

2019 Multiscale Modeling Consortium Meeting - Translation and Dissemination (March 6-7, 2019)

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Institution(s): University of Virginia

MSM U01 Grant Number: HL127654

Title of Grant: Multiscale Models of Cardiac Growth, Remodeling, and Myocardial Infarction

Abstract Authors

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Abstract Text

Introduction

Heart failure increases the likelihood of conduction abnormalities such as left bundle branch block (LBBB), which causes uncoordinated contraction and dilation of the left ventricle, leading to reduced pump efficiency [1,2]. In the last two decades, cardiac resynchronization therapy (CRT) has emerged as a revolutionary therapy for patients with heart failure and LBBB. When it works, CRT can stop and even reverse the progression of heart failure, reducing the ventricle size and improving pump function. However, over 35% of patients still fail to respond to CRT [3]. One of the greatest strengths of CRT is that it can be customized to individual patients. Yet this also presents a dilemma: there are far too many possible lead locations and pacing settings to test directly during the implantation surgery. Computational models can address this challenge by rapidly screening many pacing options before the CRT takes place. These models could be used to pre-identify pacing locations which lead to the greatest long-term predicted reduction in ventricular volume. In this study, we propose a computational framework that can provide fast, patient-specific predictions of cardiac growth after the onset of LBBB. Furthermore, we demonstrate that our model's initial growth predictions agree with previously published experiments.

Methods

The mechanics of the left ventricle (LV) were modeled using a recently published compartmental model that was coupled to a circuit model of the circulation to simulate hemodynamics throughout the cardiac cycle [4]. This framework was extended to simulate LBBB by functionally splitting the LV into 10 compartments [5]. To determine the mechanical activation time for each compartment, we used DENSE MRI to measure the local time of onset for circumferential shortening throughout the LV wall in a dog one week after inducing LBBB using radiofrequency ablation. Cardiac growth was modeled by a previously published [6] and calibrated [4] strain-based kinematic growth relation that allows for independent growth in the circumferential and radial direction. No changes to the growth parameters were made for this study. To validate our model, we compared our results to experimental data published by Vernooij et al. [1]. In brief, they used radiofrequency ablation to induce LBBB in dogs, and performed echocardiography measurements at baseline and every two weeks over a 16-week period after LBBB onset to obtain changes in LV end-diastolic volume (EDV) and wall volume.

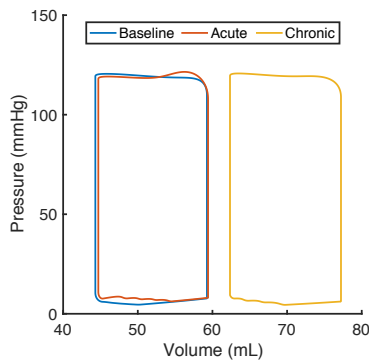


Figure 1: The pressure-volume relationship of the LV remained similar to baseline acutely after the onset of LBBB, but shifted to the right following growth.

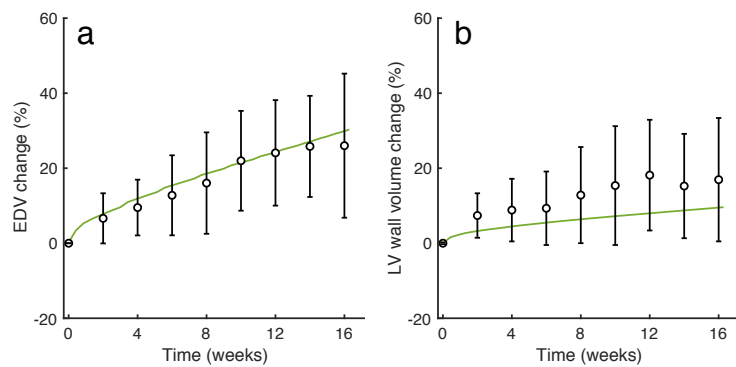


Figure 2: Predicted increases (green lines) in LV EDV (a) and wall volume (b) fell well within the range of the standard deviation of published experimental data [1].

Results

16 weeks of strain-driven cardiac growth after the onset of LBBB were simulated in just under two minutes on a laptop computer. Our model results showed that, immediately after simulating LBBB, the pressure-volume loop of the total LV was similar to baseline (Figure 1). After 16 weeks of cardiac growth the pressure-volume loop shifted to the right. Without re-calibrating any of the growth parameters in a model that was previously fitted to pressure-overload and volume-overload experiments, the model-predicted evolution of EDV closely matched the experimental results (Figure 2a). The change in LV wall volume at end diastole also fell within the standard deviation of the experimental results (Figure 2b).

Discussion

The initial results of our model matched previously reported experimental results. Strikingly, this was achieved without calibrating any of the growth parameters, instead using parameters that were previously fitted to cardiac pressure- and volume-overload data [4]. Furthermore, our model simulated 16 weeks of cardiac growth in just under two minutes on a laptop computer, making it suitable for routine clinical use. In contrast, a previously published anatomically realistic finite-element model was only able to correctly capture growth during LBBB after changing hemodynamic parameters, and required 3 weeks on a cluster with 12 6-core processors to simulate 4 weeks of growth [6,7]. In conclusion, in the present study we demonstrated that cardiac growth, in particular LV dilation, during dyssynchrony can be predicted using a fast computational model. While this work represents just the first step towards predicting patient-specific CRT responses, we believe both the results and the time frame required to customize and run this model suggest promise for this approach in a clinical setting.

References

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